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PRINCIPAL INVESTIGATOR: Anatoly Dritschilo, MD

CONTRACTING ORGANIZATION:
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14. ABSTRACT

The training grant has two goals. The first goal is to integrate the students from Hampton University (HU) into the Prostate Center through research, lectures, seminars, and clinical exposure. The second goal is to attract talented HU students into the graduate prostate cancer program at GU. To achieve these goals, the training program is divided into two parts. Part I (8-12 weeks) consists of a mentored summer research experience at GU in the laboratory of a training faculty and attendance of lectures, seminars, and journal club. Attendance on clinical rounds and at clinical conferences on prostate cancer allows the trainees to follow prostate cancer patients through treatment. In addition, the trainees attend the weekly graduate school preparation session and are scheduled to take the GRE general and subject tests. During the academic year, part II consists of an educational and research component that enhances the prostate cancer training of the students through enrollment in HU BIO408 – Research Problems. During the first year of funding, four students from HU conducted research on the mechanism of action of novel drugs that sensitize prostate tumors to radiation treatment; on the role of metals in the activation of the androgen receptor; differences in protein signatures of prostate cancer cells from African and European Americans; and the status of PTEN gene deletion and expression and TMPS22 translocations in conditionally re-programmed prostate cancer cell lines. The students are currently enrolled in the Research Problems course and scheduled to take the GRE exam.

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INTRODUCTION

The Lombardi Comprehensive Cancer Center (LCCC) at Georgetown University (GU) is a National Cancer Institute designated Comprehensive Cancer Center. The Prostate Center at LCCC has a multidisciplinary clinic where physicians and scientists interact to advance state-of-the-art treatment of patients with the goal of curing prostate cancer and maximizing quality of life. Urological surgeons, radiation oncologists, population scientists, medical oncologists, patient advocates, and basic scientists work together to develop clinical protocols that translate laboratory and technical discoveries to the clinic. Scientists at the Prostate Center are working to discover the molecular causes of prostate cancer and the population-wide impact of the disease. Their research is grouped into several thematic areas including prevention, detection and diagnosis, advancing treatment, and survivorship. Hampton University (HU), founded in 1869, is a dynamic, progressive institution of higher education that is a privately endowed, non-profit, non-sectarian, co-educational, historically black university. The Department of Biological Sciences has over 400 students and offers both the B.Sc and M.Sc. degrees. The Department is second among HBCU's in the number of B.Sc. degrees granted and is ranked nineteenth among all schools in the U.S. The Department boasts a 100% retention rate. The training grant has two goals. The first goal is to integrate the students from Hampton University into the Prostate Center through research, lectures, seminars, and clinical exposure. The second goal is to attract talented HU students into the graduate prostate cancer program, particularly at Georgetown University. To achieve these goals, the training program is divided into two parts. Part I (8-12 weeks) consists of a mentored summer research experience at GU in the laboratory of a training faculty and attendance of lectures, seminars, and journal club that provides a comprehensive scientific foundation in prevention, etiology, and initiation of prostate cancer through the progression and metastasis of the disease. Attendance at clinical rounds and at clinical conferences concerning prostate cancer allows the trainees to better understand prostate cancer treatment. In addition, the trainees attend a weekly graduate school preparation session and are scheduled to take the GRE general and relevant subject tests. During the academic year at Hampton University, Part II consists of an educational and research component that enhances the prostate cancer training of the students through enrollment in HU BIO408 – Research Problems. This class consists of seminars/lectures given by the HU and GU training faculty. In addition, the HU faculty oversee a prostate cancer research projects and assist in development of research poster presentations.

***KEY WORDS**:* prostate cancer, undergraduate training, underrepresented minorities

OVERALL PROJECT SUMMARY

During the second year of funding, we successfully recruited four additional very talented undergraduate from Hampton University to spend the summer participating in prostate cancer research at Georgetown University. In addition to working on research projects, the students participated in seminars and prepared to take the GRE exam. The students are currently enrolled in the Research Problems course at Hampton

University and registered to take the GRE exam this semester if this goal has not already been accomplished.

KEY RESEARCH ACCOMPLISHMENTS *September 2014 to September 2015*

Aim 1 – Foster collaborations between Georgetown University and Hampton University that will lead to the recruitment of Hampton University undergraduate students into the prostate cancer training program at Georgetown University Medical Center.

Task 1. Recruitment of Hampton University undergraduate students:

A. Recruitment:
1. Drs. Kenney and Ricks-Santi recruited four third year undergraduate students from the Department of Biological Sciences at Hampton University for the summer of 2015. The students included Ms. Tyanna Jones-Gray (Dr. Vicente Notario), Ms. Damara Miller (Dr. Eliot Rosen), Ms. Jasmine Hatcher-Moorman (Dr. MaryBeth Martin), and Mr. Isaiah Brown (Dr. Anatoly Dritschilo).

B. Selection:
1. The students were selected based on their research interests, overall and science GPA, and letters of recommendation.

Task 2a. Placement of Hampton University undergraduate students in Georgetown University mentor's laboratory:

1. Based on their research interest, the Hampton students indentified potential mentors in the GUMC prostate program.

2. Potential Georgetown University mentors were then contacted. Hampton University students were also be given the contact information of undergraduate, graduate, and postdoctoral trainees in the mentor's laboratory and encouraged to contact the mentor's trainees.

Task 2b. Provide Hampton University students with rigorous coursework in cancer biology methods during the academic year:
Course coordinator:
Luisel Ricks-Santi, PhD
Associate Professor
Department of Biological Sciences
Director, Cancer Research Center
Hampton University
Hampton, VA 23668

Academic Catalog Course Description- BIO 423 Cancer Biology Laboratory. Laboratory course on principles of cancer biology and fundamental techniques by which to investigate biochemical and molecular end-point responses of normal and cancer

cells. Designed to provide hands-on laboratory research experience that will strengthen the ability of students to develop testable scientific hypotheses and skills in data analysis. Prerequisite: BIO 105 and consent of instructor.

Applied Course Description – The goal of this course to identify the differences between normal cells and cancer cells using techniques commonly used in molecular biology. This course will effectively train students to identify the appropriate technique for a given research question with a focus on some of the hallmarks of cancer. Those hallmarks are: (1) cancer cells stimulate their own growth; (2) they resist inhibitory signals that might otherwise stop their growth; (3) they resist their own programmed cell death (apoptosis); (4) they stimulate the growth of blood vessels to supply nutrients to tumors (angiogenesis); (5) they can multiply forever; (6) they invade local tissue and spread to distant sites (metastasis); (7) abnormal metabolic pathways; (8) evading the immune system; (9) chromosome abnormalities and unstable DNA; and (10) inflammation.1,2
This lab will also reinforce understanding of the central dogma (Figure 1) – the flow of information from DNA to RNA to protein to phenotype, through comparing the phenotype of lung cancer cells from a smoker and a patient who never smoked. The lab will address basic principles in cell and molecular biology, including chemistry, cell structure and function, transcription and translation, enzymes, and principles of cell cycle regulation. The lab will also provide an opportunity to discuss relevant issues in society today (e.g., prostate cancer prevention and treatment, health care disparities) and why prostate cancer is so difficult to treat (e.g. not just one disease, as illustrated by the different genetic changes in the two cancer cell lines that are investigated).

Lab theme: Prostate Cancer
Prostate cancer (PCa) is the most common non-skin cancer and the second leading cause of cancer death among men in the United States (US) [1]. Although there are three well-established risk factors for prostate cancer, age, ethnicity, and family history [2], the molecular mechanisms underlying its development and progression remain poorly understood. Additionally, the factors influencing disparities of PCa in African American (AA) men also remain poorly understood as AA men have the highest mortality rate for PCa of any racial or ethnic group in US. The wide variation observed in the incidence of PCa and mortality rates in AA men are suggested to be multifactorial, with varying effects of genetic predisposition, diet, and other environmental factors. One approach that can help improve characterization of PCa tumors is to identify the molecular mechanisms that drive the aggressive phenotype and to identify the genes associated with aggressive, high Gleason (grade) PCa. So far, molecular analysis of PCa tumors have resulted in the identification of genomic markers associated with adverse outcomes and several groups have attempted to develop genomic profiles that can predict PCa aggressiveness [3-10].

Required Textbook(s) and materials- This course will use the publications and informational pamphlets:
1. Hanahan D, Weinberg RA (January 2000). "The Hallmarks of Cancer". Cell 100 (1):57–70. doi:10.1016/S0092-8674(00)81683-9. PMID 10647931
2. Hanahan, D. & Weinberg R.A. (2011) “Hallmarks of Cancer: The Next Generation”. Cell 144 (5): 646-674. Doj: 10.1016/j.cell.2011.02.013. PMID 21376230
3. 3-ring binder to place lab guides in.

4. Composition notebook to be used as a lab notebook. If you prefer, you can use Microsoft OneNote as an eLab notebook to write up your labs and keep your notes.

Recommended Reading (as cited in Lab Theme):

1. American Cancer Society, Cancer Facts and Statistics 2014. 2014.
2. Rodriguez C, Calle EE, Miracle-McMahill HL, Tatham LM, Wingo PA, Thun MJ, Heath CW, Jr.: Family history and risk of fatal prostate cancer. Epidemiology 1997, 8:653-657.
3. Klein EA, Cooperberg MR, Magi-Galluzzi C, Simko JP, Falzarano SM, Maddala T, Chan JM, Li J, Cowan JE, Tsiatis AC, Cherbavaz DB, Pelham RJ, Tenggara-Hunter I, Baehner FL, Knezevic D, Febbo PG, Shak S, Kattan MW, Lee M, Carroll PR: A 17-gene Assay to Predict Prostate Cancer Aggressiveness in the Context of Gleason Grade Heterogeneity, Tumor Multifocality, and Biopsy Undersampling. Eur Urol 2014.
4. Bibikova M, Chudin E, Arsanjani A, Zhou L, Garcia EW, Modder J, Kostelec M, Barker D, Downs T, Fan JB, Wang-Rodriguez J: Expression signatures that correlated with Gleason score and relapse in prostate cancer. Genomics 2007, 89:666-672.
5. Singh D, Febbo PG, Ross K, Jackson DG, Manola J, Ladd C, Tamayo P, Renshaw AA, D'Amico AV, Richie JP, Lander ES, Loda M, Kantoff PW, Golub TR, Sellers WR: Gene expression correlates of clinical prostate cancer behavior. Cancer Cell 2002, 1:203-209.
6. Cheville JC, Karnes RJ, Therneau TM, Kosari F, Munz JM, Tillmans L, Basal E, Rangel LJ, Bergstralh E, Kovtun IV, Savci-Heijink CD, Klee EW, Vasmatzis G: Gene panel model predictive of outcome in men at high-risk of systemic progression and death from prostate cancer after radical retropubic prostatectomy. J Clin Oncol 2008, 26:3930-3936.
7. Cuzick J, Berney DM, Fisher G, Mesher D, Moller H, Reid JE, Perry M, Park J, Younus A, Gutin A, Foster CS, Scardino P, Lanchbury JS, Stone S: Prognostic value of a cell cycle progression signature for prostate cancer death in a conservatively managed needle biopsy cohort. Br J Cancer 2012, 106:1095-1099.
8. Amaro A, Esposito AI, Gallina A, Nees M, Angelini G, Albini A, Pfeffer U: Validation of proposed prostate cancer biomarkers with gene expression data: a long road to travel. Cancer Metastasis Rev 2014.
9. Rabiau N, Dantal Y, Guy L, Ngollo M, Dagdemir A, Kemeny JL, Terris B, Vieillefond A, Boiteux JP, Bignon YJ, Bernard-Gallon D: Gene panel model predictive of outcome in patients with prostate cancer. OMICS 2013, 17:407-413.
10. Erho N, Crisan A, Vergara IA, Mitra AP, Ghadessi M, Buerki C, Bergstralh EJ, Kollmeyer T, Fink S, Haddad Z, Zimmermann B, Sierocinski T, Ballman KV, Triche TJ, Black PC, Karnes RJ, Klee G, Davicioni E, Jenkins RB: Discovery and validation of a prostate cancer genomic classifier that predicts early metastasis following radical prostatectomy. PLoS One 2013, 8:e66855.

Specific Intended Student Learning Outcome(s) - By the end of this course, students will be able to describe, compare, select, and perform, appropriate molecular methods for cancer research using Scientific Reasoning and Critical Thinking core competencies.

General Instructional Objectives (Goals)

- Define basic terminology and describes concepts in molecular genetics that provide the foundation for implementing and adapting new techniques and assays in cancer research; this will be assessed through lab reports and final exam.
- Determine the difference between normal and cancer cells; this will be assessed through lab reports and final exam.
- Describe the principles of nucleic acid isolation and successfully perform isolations; this will be assessed through successful performance of the lab and the final exam.

- Describe the principles of polymerase chain reaction (PCR), reverse transcriptase PCR and other amplification techniques; this will be assessed through successful performance of the lab and the final exam.
- Describe the principles of nucleic acid electrophoresis and hybridization including Southern and Northern blots; this will be assessed through the final exam.
- Define SNPs and explain the principle of RFLP in genotyping; this will be assessed through successful performance of the lab and the final exam.
- Describe the principles of cytogenetics and fluorescent in situ hybridization (FISH); this will be assessed through successful performance of the lab and the final exam.
- Describe the principles of Immunohistochemistry, ELISA, and Western blot; this will be assessed through successful performance of the lab and the final exam.
- Interpret results in context of other laboratory data; this will be assessed through lab reports.
- Record and communicate cancer research results in a professional manner; this will be assessed through lab reports.

Week of	Topic	Assignment Due
15-January	Introduction to course, syllabus, and lab safety	
22-January	Lab 1. Measurements and Micropipetting	
29-January	Lab 2. Microscopy and cell culture lab	Lab notebook due
5-February	Lab 2. Microscopy and cell culture lab	
12-February	Lab 3. Protein extraction lab	Lab notebook due
19-February	Lab 3. Coomassie blue staining	
26-February	Lab 3. Western Blot lab	
5-March	Lab 4. Solutions and Dilutions	Lab notebook due
19-March	Lab 4. DNA isolation lab	
26-March	Lab 4. PCR lab	
2-April	Lab 4. Agarose gel electrophoresis lab	
9-April	Lab 5. Gene Expression	Lab notebook due
16-April	Presentations	
TBD	Final Presentations	

Print Self-Evaluation	Complete assignment in notebook	Virtual Lab
		sign up http://amrita.vlab.co.in/index.php?pg=bindex&bsub=login_page
√	√	Light Microscope http://amrita.vlab.co.in/index.php?sub=3&brch=187&sim=323&cnt=1
√	√	Preparation of Buffer stocks (TBE,TE and TAE) http://amrita.vlab.co.in/index.php?sub=3&brch=77&sim=1322&cnt=1
√	√	Western Blotting http://amrita.vlab.co.in/index.php?sub=3&brch=187&sim=1331&cnt=1
√	√	Polyacrylamide Gel Electrophoresis http://amrita.vlab.co.in/index.php?sub=3&brch=186&sim=319&cnt=1
√	√	Maintenance of Mamallian Cell Lines http://amrita.vlab.co.in/index.php?sub=3&brch=188&sim=331&cnt=1

√ √ Cell Proliferation
http://amrita.vlab.co.in/index.php?sub=3&brch=188&sim=1101&cnt=1
√ √ Hemocytometer (Counting of Cells)
http://amrita.vlab.co.in/index.php?sub=3&brch=188&sim=336&cnt=1

√ √ Extraction of DNA from Fish Fins
http://amrita.vlab.co.in/index.php?sub=3&brch=77&sim=218&cnt=1
√ √ Agarose Gel Electrophoresis (AGE)
http://amrita.vlab.co.in/index.php?sub=3&brch=77&sim=1375&cnt=1
√ √ Polymerase Chain Reaction (PCR)
http://amrita.vlab.co.in/index.php?sub=3&brch=186&sim=321&cnt=1

√ √ Isolation of RNA
http://amrita.vlab.co.in/index.php?sub=3&brch=186&sim=718&cnt=1

Task 3. Georgetown University provided a summer research and training program for Hampton University undergraduate students:

1. The Hampton University undergraduates (Ms. Tyanna Jones-Gray, Ms. Damara Miller, Ms. Jasmine Hatcher-Moorman, and Mr. Isaiah Brown) conducted prostate cancer research (8 - 12 weeks) in the laboratory of a Georgetown University mentor (Drs. Notario, Rosen, Martin and Dritschilo, respectively).

2. Hampton University trainees participated in and presented their research at weekly laboratory research data meetings.

3. The trainees attended the weekly Brown Bag Lunch Lecture. (Schedule with topics in Appendix)

4. The trainees also attended Oncology Grand Rounds, the weekly Oncology Journal Club and Seminar, and the weekly Oncology Faculty Seminar. (Schedule with topics in Appendix)

5. Trainees attended a weekly graduate school preparation session and are scheduled to take the GRE general and subject tests in the Fall of 2015. The trainees from the summer of 2015 will take the tests in the Fall of 2015.

Task 4. Georgetown University faculty participated in teaching the Hampton University undergraduate course HU BIO408 – Research Problems:

1. Hampton University undergraduate students who participated in the summer of 2015 are currently enrolled in HU BIO423 Cancer Biology Laboratory. Dr. Ricks-Santi's HU423 course presents various aspects of clinical and basic cancer research in a lecture format (50 minutes) which is detailed in this report under Task 2B.

Task 5. Hampton University faculty advisor provided prostate cancer research opportunities for the undergraduate trainees:

1. The Hampton University faculty advisors are providing *in vitro* and genomic research opportunities in prostate cancer during the academic year for the undergraduate trainees via enrollment in HU BIO408 Research Problems.

Task 6. Georgetown University faculty provided continuing prostate cancer summer research opportunities for Hampton University undergraduate trainees:

1. Mr. Myron Gilbert, one of the Hampton students returned to Georgetown the following summer to continue his research project.

Task 7. Georgetown University will continue to track the career progress of the Hampton University undergraduate students:

The career progress of the Hampton University students is being tracked by the Office of Cancer Research Education of the Lombardi Comprehensive Cancer Center of Georgetown University. Currently, the students from the summer of 2015 are seniors at Hampton University and are expected to graduate in May 2016. Several students from the summer of 2014 are also graduating in May 2016. A number of these students are in the process of applying to graduate programs. Shannon Anderson, a student from the summer of 2014 graduated in May of 2015 from Hampton University and is currently enrolled in the Georgetown University/George Mason University joint program in Physiology.

PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS

In Dr. Notario's laboratory, Tyanna Jones-Gray research project focused on the study of the molecular mechanisms of oncogenesis and involved the investigation of the effects of environmental carcinogens such as ionizing radiation on prostate cancer cells with regard to the expression and activity of cancer genes and their protein products. Dr. Notario's research group isolated and investigates the role of a novel oncogene, termed PCPH, which is conserved in eukaryotic cells from yeast to humans, and cooperates with other oncogenes such as H-ras in the neoplastic transformation of mammalian cells. Ms. Jones-Gray studied the effects carcinogens on the expression of PCPH.

In Dr. Rosen’s laboratory, Damara Miler studied the signal transduction pathways of scatter factor and its receptor c-Met that lead to resistance to radiation and chemotherapy. Her project focused on the role of Met pathway in cancer progression.

Dr. Martin’s lab has identified the environmental hormones referred to as metallo-hormones. In Dr. Martin’s laboratory, Jasmine Hatcher-Moorman studied the role of metals in the development of prostate cancer and defined the mechanism by which metals activate the androgen receptor.

Dr. Dritschilo’s laboratory is developing new drugs and radiation sensitizing agents for the treatment of prostate cancer. While in Dr. Dritschilo’s laboratory, Isaiah Brown worked on the development of histone deacetylase inhibitors and small molecules that

abrogate the interaction between Raf-1 and Ras and thereby sensitize prostate cancer cells to radiation.
The students will have the opportunity to present their research at the Student Research Day at Hampton University and will be encouraged to present their research at the Student Research Day at Georgetown University in the Spring of 2016.

INVENTIONS, PATENTS AND LICENSES - nothing to report

REPORTABLE OUTCOMES – nothing to report

OTHER ACHIEVEMENTS

Preliminary data generated by Ashton Green was used in a grant application to the DOD for an IDEA Award in prostate cancer.

REFERENCES – none

APPENDICES to Follow - Schedules and Topics for Brown Bag Lunch Seminars and Grand Rounds lectures for Summer 2015. Students attended these educational offerings as part of the training program.

CANCER BIOLOGY
&
CANCER SYSTEMS BIOLOGY SEMINAR SERIES

SCHEDULE: SUMMER 2015

Location: W302, NRB
Time: Tuesdays – Noon - 1:00 pm

June 16	**Overview of Cancer** **Louis Weiner, M.D.** **Director of Lombardi Cancer Center**
June 23	**Overview of Cancer Systems Biology** **Robert Clarke, Ph.D.** **Dean for Research**
June 30	**Viruses and Cancer** **Hang Yuan, Ph.D.** **Associate Professor of Oncology**
July 7	**Cancer Prevention** **Leena Hilakivi-Clarke, Ph.D.** **Professor of Oncology**
July 14	**Metabolomics as a new tool in cancer systems biology** **Amrita Cheema, Ph.D.** **Associate Professor of Oncology**
July 21	**Cancer Drug discovery** **Milton Brown, M.D./Ph.D.** **Director of Drug Discovery**
July 28	**Vaccine Development** **Richard Schlegel, M.D./Ph.D.** **Chairman of Pathology**
August 4	**Career paths in science and medicine that lead to novel (potential) therapeutics** **Jeffrey Toretsky, M.D.** **Professor of Oncology**

Coordinator: Mira Jung, Ph.D. for Cancer Biology (jungm@georgetown.edu)
Ayesha Shajahan-Haq, Ph.D. for Cancer Systems Biology (ans33@georgetown.edu)

2014 Brown Bag Cancer Systems Biology Seminar Series

Sponsored by the Georgetown Center for Cancer Systems Biology (CCSB)

POC: Ayesha N. Shajahan-Haq, PhD (email: ans33@georgetown.edu)

Location: W302, Research Building

Time: Thursdays, 12:00pm-1:00pm

Date	Speaker	Topic
June 19	Robert Clarke	A systems biology approach to understanding drug resistance in breast cancer
June 26	Amrita Cheema	Metabolomics as a new tool in cancer systems biology
July 10	Difei Wang	Connecting the dots – methods and tools for integration of multiple data types for molecular profiling of cancer
July 17	Nathan John Edwards	Gene Set Enrichment and Splicing Detecting using Spectral Counting
July 24	Anne Deslattes Mays	RNA-seq and Differential Expression Profiling
July 31	William T. Baumann	Mathematical modeling of cancer cells: How?, why?, and will it work?
August 7	Habtom Ressom	Metabolite Identification: a bottleneck in LC/MS-based metabolomic studies